UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,176	06/18/2001	Christian Reiter	105032-991190	3010

35928 7590 08/13/2003

GRAY CARY WARE FREDENRICH
1625 MASSACHUSETTS AVENUE, NW
SUITE 300
WASHINGTON, DC 20036-2247

EXAMINER
LI, BAO Q

ART UNIT	PAPER NUMBER
1648	15

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,176	REITER ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,17 and 22-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,17 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

This is a response to the amendment, paper No. 11, filed 05/09/03. The amendment of specification has been entered. Claims 1-4 and 17 have bee amended. Claims 5-16, and 18-21 have been canceled. New claims 22-24 are added. Claims 1-4, 17 and 22-24 are pending and considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-4, 17 and 22-24 are still rejected under 35 U.S.C. 112, second paragraph on the same ground as stated in the previous Office Action, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 1 is still rejected for being unclear and confusing in that the claim fails to define precisely what at least one and other complementary determining regions (CDR) of the V_H and V_L are. Applicants are reminded that the method for making a monoclonal antibody or chimeric antibody or an antibody fragment by CDR grafting requires **3 pairs of defined CDRs and four defined framework regions (FRs)** in combination with constant regions to create variety of an antibody that bind to the same antigen epitope, wherein the defined 3 CDRs and FRs form a loop-like structure for contacting with an antigen, holding it in place as taught by Bendig et al. (METHODS: A companion to Methods in Enzymology 1995, Vol. 8, pp. 83-93).

4. Applicants transverse the rejection and submit that the references of Laune et al. and Feng et al. provided by Applicants teach that a single CDR is sufficient for obtaining specific binding.

5. Applicants' argument has been respectfully considered; however, it is not found persuasive because neither Laune et al. nor Feng et al. teach that the only one CDR can make a defined antibody. What they teach is a peptide (antigen), but not antibody, containing at least one or several the CDR binding regions.

6. During the telephone interview with Attorney Nakamura et al. on July 30, 2003, Applicants are suggested to amend the claims with 3 pairs of CDRs and 4FRs (SEQ ID NO) to overcome the rejection. Otherwise, the claim is considered indefinite. This rejection affects the dependent claims 2-4, 17 and 23-24.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-4, 17 and 22-24 are still rejected under 35 U.S.C. 112, first paragraph on the same ground as stated in the previous Office Action, because the specification, while being enabling for having a human anti-HCV E2 antibody having a defined V_L of SEQ ID NO: 2 and a defined V_H of SEQ ID NO: 4, wherein the antibody is able to bind the HCV E2 antigen, precipitate the E1/E2 associated complex, and block the E2 binding to the target cells, does not reasonably provide enablement for making an antibody with only one complementarity determining region of V_H or V_L region that is able to make any or all same antibody with an ability to bind the HCV E2 antigen, precipitate the E1/E2 associated complex, and block the E2 binding to the target cells . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

9. Applicants transverse the rejection and submit that examiner has not made out a pima facie case of non-enablement because Applicants indicate that the claims have been amended

with a sequence and references provided by Applicants teach that at least one CRD is sufficient to practice the instant invention.

10. Applicants' argument has been respectfully considered; however, it is not persuasive because the references provided by Applicants do not teach that antibody with only one CDR is able to make any or all same antibody with same binding ability. For example, both Launet and Feng teach that the peptides (antigen), but not antibody, contain one or several the CDR binding region. The CDR regions are required sequence domains in the antibody molecule but not in the antigen as described in the previous Office Action.

11. During the telephone interview with attorney Dean H. Nakamura on July 30, 2003, office suggest that Applications to amend the claims with 3 pairs of CDR sequence of CDR for claimed antibody for overcoming the outstanding rejection.

Claim Rejections - 35 USC § 102

12. Claims 2, 4 and 22 are still rejected under 35 U.S.C. 102(a) as being anticipated by Nakano et al. (J. Virol. 1997, Vol. 71, pp. 7101-7109) on the same ground as stated in the previous Office Action.

13. Applicants argue that Nakano et al.'s disclosure is related to a linear epitope because Applicants presumably believe that the antibody disclosed by Nakano react in an ELISA assay.

14. Applicants argument has been fully considered; however, it is not found persuasive because the antibodies disclosed by Nakada et al. do not only react with the linear antigen epitopes in ELISA assay, but also be able to immunoprecipitate the HCV E1/E2 antigen complex in western blot assay, in which the E2 antigen epitope is not only presented in a linear form (See Fig. 3 on page 7105 and Fig. 5 on page 7106). Therefore, the rejection is maintained.

15. Claims 4, 17, 22 and 23-24 are still rejected under 35 U.S.C. 102(b) as being anticipated by Persson et al. (WO 97/40176) on the same ground as stated in the previous Office Action.

16. Applicants transverse the rejection and submit that the homology of the Personn's antibody' variable heavy chains between the light chains are different from that of current Application; they are assuming that the two antibodies cannot be identical.

17. Applicants' argument has been fully considered; however, it is not found persuasive because the rejected claims invention is directed an isolated antibody that can recognize E2

antigen conformation epitope and neutralize the E2 binding to the target cell. The different homology of H_V and L_V between two antibodies does not necessarily mean that the two antibodies cannot recognize same antigen epitope. To the contrary of Applicants' argument, the antibodies disclosed by Persson et al. are not only able to recognize the E2 antigen epitope in an ELISA assay but also precipitate E1/E2 antigen complex. Furthermore, Persson also teach that an isolated antibody or fragment is able to block the HCV E2 binding to the target cells. All these characteristics of the antibodies disclosed by Personn et al. meet the limitations of claimed antibodies in claims 4, 17 and 22. In addition, the neutralizing assay disclosed by Persson et al. also anticipates the claims 23 and 24. Unless Applicants amend the claims with a precise defined antigen-binding epitope (SEQ ID NO) or defined CDR sequences, the rejection is maintained.

18. Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by Cardoso et al. (J. Med. Virol. 1998, Vol. 55, pp. 28-34) on the same ground as stated in the previous Office Action.

19. Applicants transverse the rejection and argue that the antibodies disclosed by Cardoso et al. bind to HCV genotypes 1a and 1b, whereas, the specification of the instant application states that the antibodies of interest in the current application bind to different genotypes, such as 2a, 3a and 4.

20. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., binding to different genotypes of HCV 2a, 3a and 4) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claim 4 is still rejected under 35 U.S.C. 102(b) as being anticipated by Deleersnyder et al. (J. Virol. 1997, Vol. 71, pp. 697-704) on the same ground as stated in the previous Office Action.

23. Applicants transverse the rejection and submit that the antibody disclosed by Deleersnyder et al. is directly against E1/E2 complex of HCV genotype 1a, whereas the antibody of the instant Application recognize an epitope located on E2.

24. Applicants' argument has been respectfully considered; however, it is not found persuasive because the antibody disclosed by Deleersnyder et al. is able to recognize the same E2 antigen and to precipitate E1/E2 antigen complex (See entire document), which is just a characteristic of claimed antibody recited in claim 1, which recited that the claimed antibody precipitates covalently on non-covalently associated with E2/E2 complex. While the antibody CD may differ, an antibody may still be able to bind same antigen and has same characteristics. Therefore, the rejection is maintained.

25. Claims 4 and 22 are still rejected under 35 U.S.C. 102(b) as being anticipated by Rosa et al. (P.N.A.S. USA, 1996, Vol. 93, pp. 1759-1765) on the same ground as stated in the previous Office Action.

26. Applicants transverse the rejection and submit that the polyclonal antibodies disclosed by Rosa et al. directed against HCV E2 glycoprotein of 2a and 3s genotype and the monoclonal antibody recognize the HCV E2 protein of genotype 1a. Whereas, some of the exemplified antibodies of the instant Application were from two patients infected with HIV genotype 4 or 1b. The claimed antibodies cross-react with E2 antigens derived from the genotype 1a of HCV suggesting that the determinant(s) targeted by the claimed antibodies are conserved among at least two main prevalent viral subtype fond in the world (subtypes 1a and 1b). Applicants further argue that the antibodies of current application are likely directed at conformation-dependent domain of E2 because they display strong NOB. Therefore, these domains are conserved among different genotypes. Hence, Rosa et al. do not teach the claimed invention.

27. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the binding domains of claimed antibodies are conserved among different genotypes) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations

from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

28. Moreover, since the antibodies disclosed by Rosa et al. are able to recognize the same E2 antigen, to precipitate E1/E2 antigen complex, and block the HCV E2 binding to the target cells (See entire document), which meet all limitations of claimed antibodies in claims 4 and 22. Therefore, the rejection is maintained.

New Ground of Rejection

Claim Rejections - 35 USC § 101

29. Claim 22 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

30. In the instant case, claim 22, as written, do not sufficiently distinguish over antibodies as they exists naturally because claim 22 do not particularly point out any non-naturally occurring differences between the claimed antibody and binding composition and the structure of naturally occurring antibodies. It is well known that in during the HCV infection, antibodies against HCV E2 antigen are generated and the claims as currently recited encompass these naturally occurring compositions.

31. In the absence of the hand of man, the naturally occurring antibodies are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claim to recite "an isolated or purified" antibody or similar language would obviate this rejection.

32. No claims are allowed.

Conclusion

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

2. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

4. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

5. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
Art Unit 1648
August 9, 2003